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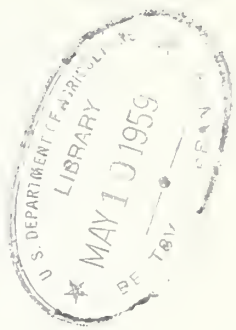

SCREENING TESTS OF SUBSTITUTED BENZYL AND NAPHTHALENEMETHYL ESTERS OF CHRYSANTHEMUMIC ACID

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The results of screening tests on candidate insecticides consisting predominantly of esters containing the methylenedioxyphenyl structure have been reported in previous papers (2, 3, 4, 5). Two of the compounds, 6-bromo-and 6-chloro-piperonyl chrysanthemumates (3), exhibited pronounced insecticidal properties. This paper reports on related compounds--namely, substituted benzyl chrysanthemumates and on the intermediate compounds used in their preparation.

Four procedures for synthesizing the substituted benzyl alcohols were employed:

I. The substituted benzene was chloromethylated as already described (1, 8). The resultant benzyl chloride was converted to the corresponding acetate and saponified to give the desired benzyl alcohol, in accordance with the procedure of Barthel and Alexander (3).

II. The substituted benzoic acid was reacted in the usual manner with absolute methanol and hydrogen chloride to give its methyl ester. In compounds with a hydroxy group on the benzene ring, the group was alkylated in acetone with the desired alkyl halide in the presence of potassium carbonate and a catalytic amount of potassium iodide (Claisen 6). Reduction of the ester group with lithium aluminum hydride (Barthel and Alexander 3) gave the alcohol.

III. The methyl allyloxybenzoate, prepared as described under method II, was rearranged according to the method of Claisen and Eisleb (7). The free hydroxy group was then alkylated (this step sometimes omitted) and the ester group reduced with lithium aluminum hydride.

IV. Salicylaldehyde was converted to its allyl ether (6) and reduced with lithium aluminum hydride.

The chrysanthemumates were prepared from the alcohols by the acid chloride or transesterification route (Chen and Barthel 5).

Formulas and physical properties of these compounds are given in tables 1-5 and the results of the screening tests in table 6.

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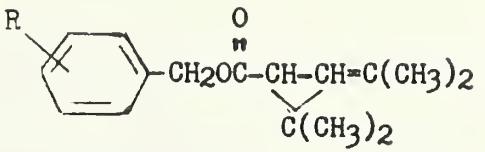
Table 1.--Substituted benzyl chrysanthemumates



ENT No.	Empirical formula	Substituent	R	Yield %	Boiling point		n_D^{25}
					°C.	mm.	
21170	$C_{19}H_{26}O_2$	2,4-dimethyl-	2,4-$(CH_3)_2$	80	175	3.8	1.5169
21171	$C_{19}H_{26}O_3$	p-ethoxy-	4-OC_2H_5	79	186-7	3.5	1.5157
21173	$C_{18}H_{24}O_3$	m-methoxy-	3-OCH_3	86	142-53	0.3	1.5195
21340	$C_{19}H_{26}O_3$	m-ethoxy-	3-OC_2H_5	87	155-62	.7	1.5150
21342	$C_{20}H_{28}O_3$	m-propoxy-	3-OC_3H_7	82	167-70	.9	1.5112
21422	$C_{20}H_{26}O_3$	m-allyloxy-	3-$OCH_2CH=CH_2$	79	173-8	.9	1.5210
21423	$C_{21}H_{30}O_2$	p-tert-butyl-	4-$C(CH_3)_3$	71	168	.8	1.5090
21424	$C_{19}H_{26}O_3$	o-ethoxy-	2-OC_2H_5	69	166-9	.9	1.5150
21425	$C_{21}H_{30}O_3$	m-isobutoxy-	3-$OCH_2CH(CH_3)_2$	48	171-8	1.0	1.5140
21426	$C_{20}H_{28}O_3$	m-isopropoxy-	3-$OCH(CH_3)_2$	82	165	1.1	1.5098
21427	$C_{20}H_{26}O_3$	o-allyloxy-	2-$OCH_2CH=CH_2$	56	173-81	1.4	1.5208
21556	$C_{21}H_{30}O_3$	p-butoxy-	4-OC_4H_9	70	166-83	0.6	1.5086
21558	$C_{19}H_{26}O_2$	p-ethyl-	4-C_2H_5	87	155-7	.9	1.5130
21559	$C_{18}H_{24}O_2$	o-methyl-	2-CH_3	88	134-55	.7	1.5157

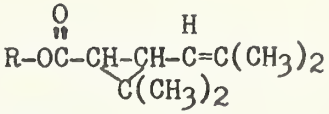
Table 1.--Continued

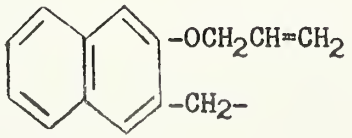
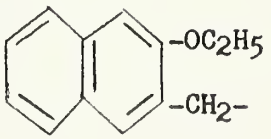
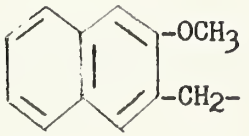
ENT No.	Empirical formula	Substituent	R	Yield %	Boiling point °C.	Boiling point mm.	n_D^{25}
21560	$C_{20}H_{28}O_3$	p-propoxy-	4-OC_3H_7	63	160-79	0.4	1.5126
21563	$C_{19}H_{26}O_2$	2,5-dimethyl-	2,5-$(CH_3)_2$	76	145-54	.6	1.5163
21564	$C_{21}H_{28}O_3$	m-(2-methylallyloxy)	3-$OCH_2C(CH_2)-CH_3$	82	173-83	.6	1.5193
21572	$C_{18}H_{24}O_2$	m-methyl-	3-CH_3	85	133-9	.6	1.5135
21573	$C_{21}H_{30}O_3$	m-sec-butoxy-	3-$OCH(CH_3)C_2H_5$	54	149-69	.5	1.5049
21577	$C_{21}H_{28}O_3$	p-(2-methylallyloxy)-	4-$OCH_2C(CH_2)-CH_3$	23	165-70	.4	1.5182
21578	$C_{21}H_{30}O_3$	p-sec-butoxy-	4-$OCH(CH_3)C_2H_5$	48	170-7	.5	1.5177
21825	$C_{19}H_{26}O_2$	3,4-dimethyl-	3,4-$(CH_3)_2$	69	151-72	.6	1.5172
21906	$C_{19}H_{26}O_2$	m-ethyl-	3-C_2H_5	76	134-46	.5	1.5088
30039	$C_{22}H_{30}O_3$	3-allyl-4-ethoxy-	3-$CH_2CH=CH_2$-4-OC_2H_5	76	169-74	.8	1.5184
30041	$C_{21}H_{28}O_3$	3-allyl-4-methoxy	3-$CH_2CH=CH_2$-4-OCH_3	79	164-7	.5	1.5245
30166	$C_{21}H_{30}O_4$	3-methoxy-2-propoxy-	2-OC_3H_7-3-OCH_3	69	170-86	.8	1.5110
30167	$C_{21}H_{28}O_4$	2-allyloxy-3-methoxy-	2-$OCH_2CH=CH_2$-3-OCH_3	52	151-61	.4	1.5111

30239	$C_{22}H_{30}O_3$	4-methoxy-3-(2-methylallyl)-	$3\text{-}CH_2\overset{CH_2}{\overset{\|}{C}}\text{-}CH_3\text{-}4\text{-}OCH_3$	1/	Not distilled	1.5183
30298	$C_{22}H_{30}O_3$	3-methoxy-4-(2-methylallyl)-	$3\text{-}OCH_3\text{-}4\text{-}CH_2\overset{CH_2}{\overset{\|}{C}}\text{-}CH_3$	1/	do.	1.5190
30300	$C_{21}H_{28}O_3$	o-(2-methylallyloxy)-	$2\text{-}OCH_2\overset{CH_2}{\overset{\|}{C}}\text{-}CH_3$	1/	do.	1.5127
30302	$C_{23}H_{26}O_2$	p-phenyl-	$4\text{-}C_6H_5$	1/	do.	1.5476

1/ Quantitative crude-product yield.

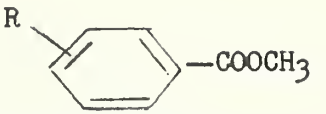
Table 2.--Substituted 2-naphthalenemethyl esters of chrysanthemumic acid[1/]



ENT No.	Empirical formula	Ester	R	n_D^{25}
30230	$C_{24}H_{28}O_3$	3-allyloxy		1.5555
30254	$C_{23}H_{28}O_3$	3-ethoxy		1.5490
30299	$C_{22}H_{26}O_3$	3-methoxy		1.5590

1/ Compounds not distilled. Crude yields quantitative.

Table 3.--Methyl esters of substituted benzoic acids



ENT No.	Empirical formula	Substituent	R	Yield %	Boiling point °C.	Boiling point mm.	n_D^{25}	Method of preparation
21001	$C_{11}H_{12}O_3$	o-(allyloxy)-	2-O-$CH_2CH{=}CH_2$	89	145	13	1.5316	II
21002	$C_{13}H_{16}O_3$	3-allyl-2-ethoxy-	2-OC_2H_5-3-$CH_2CH{=}CH_2$	50	130-4	13	1.5201	III
21009	$C_{11}H_{12}O_3$	3-allyl-2-hydroxy-	2-OH-3-$CH_2CH{=}CH_2$	55	135-44	18	1.5369	III
21310	$C_{10}H_{12}O_3$	m-ethoxy-	3-OC_2H_5	88	129-33	17	1.5173	II
21335	$C_{11}H_{14}O_3$	m-propoxy-	3-OC_3H_7	78	147-51	17	1.5120	II
21413	$C_{11}H_{12}O_3$	m-allyloxy-	3-$OCH_2CH{=}CH_2$	85	152-3	16	1.5267	II
21414	$C_{12}H_{16}O_2$	p-tert-butyl-	4-$C(CH_3)_3$	88	136-47	16	1.5095	II
21415	$C_{12}H_{16}O_3$	m-isobutoxy-	3-$OCH_2CH(CH_3)_2$	35	157-67	15	1.5228	II
21416	$C_{11}H_{14}O_3$	m-isopropoxy-	3-$OCH(CH_3)_2$	78	139-41	15	1.5070	II
21530	$C_{12}H_{14}O_3$	m-(2-methylallyloxy)-	3-$OCH_2C(CH_2)CH_3$	80	157-63	17	1.5219	II
21551	$C_{12}H_{16}O_3$	m-sec-butoxy-	3-$OCH(CH_3)C_2H_5$	57	161-72	19	1.5195	II
21552	$C_{12}H_{16}O_3$	p-sec-butoxy-	4-$OCH(CH_3)C_2H_5$	60	161-80 (m.p. 124-6)	17		II
21562	$C_{12}H_{14}O_3$	p-(2-methylallyloxy)-	4-$OCH_2C(CH_2)CH_3$	75	168-76 (m.p. 125-6)	18		II

Table 3.--Continued

ENT No.	Empirical formula	Substituent	R	Yield %	Boiling point °C	Boiling point mm.	n_D^{25}	Method of preparation
21704	$C_{11}H_{12}O_3$	p-allyloxy-	4-$OCH_2CH{=}CH_2$	57	115-28	0.5	1.5409	II
21705	$C_{12}H_{16}O_3$	p-isobutoxy-	4-$OCH_2CH(CH_3)_2$	--	164-73	17	1.5183	II
30035	$C_{12}H_{14}O_3$	3-allyl-4-methoxy-	3-$CH_2CH{=}CH_2$-4-OCH_3	73	154-63	16	1.5389	III
30036	$C_{13}H_{16}O_3$	3-allyl-4-ethoxy-	3-$CH_2CH{=}CH_2$-4-OC_2H_5	89	160-9	14	1.5287	III
30042	$C_{12}H_{16}O_3$	m-isopropoxy-	3-$OCH(CH_3)_2$	70	139-44	14	1.5000	II
30231	$C_{13}H_{16}O_3$	4-methoxy-3-(2-methylallyl)-	3-$CH_2C(CH_2){-}CH_3$-4-OCH_3	74	170-1	16	1.5320	II
30232	$C_{10}H_{12}O_4$	2,4-dimethoxy-	2,4-$(OCH_3)_2$	52	130-9	13	1.5464	II
30253	$C_{13}H_{16}O_3$	3-methoxy-4-(2-methylallyl)-	3-OCH_3-4-$CH_2C(CH_2){-}CH_3$	91	115-8	0.3	1.5267	III

Table 4.--Substituted benzyl alcohols and acetates

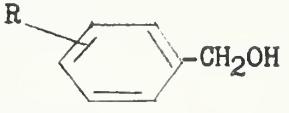
ENT No.	Empirical formula	Substituent	R	Yield %	Boiling point °C.	Boiling point mm.	n_D^{25}	Method of preparation
		Benzyl alcohols						
21159	$C_9H_{12}O$	2,4-dimethyl-	2,4-$(CH_3)_2$	96	124	18	1.5364	I
21300	$C_9H_{12}O$	3,4-dimethyl-	3,4-$(CH_3)_2$	100	126-9	17	1.5362	I
21333	$C_9H_{12}O_2$	m-ethoxy-	3-OC_2H_5	90	143-8	16	1.5330	I, II
21417	$C_{10}H_{12}O_2$	o-allyloxy-	2-$OCH_2CH=CH_2$	91	149-58	16	1.5431	IV
21418	$C_{10}H_{12}O_2$	m-allyloxy-	3-$OCH_2CH=CH_2$	94	158-62	15	1.5412	II
21419	$C_{11}H_{16}O$	p-tert-butyl-	4-$C(CH_3)_3$	85	141-2	16	1.5167	II
21420	$C_9H_{12}O_2$	o-ethoxy-	2-OC_2H_5	88	135-40	16	1.5315	II
21421	$C_{10}H_{14}O_2$	m-isopropoxy-	3-$OCH(CH_3)_2$	88	149	18	1.5213	II
21535	$C_9H_{12}O$	p-ethyl-	4-C_2H_5	67	120-3	18	1.5258	I
21536	$C_8H_{10}O$	o-methyl-	2-CH_3	77	111-4	18	1.5385	I
21555	$C_{11}H_{14}O_2$	m-(2-methylallyloxy)-	3-$OCH_2C(CH_2)-CH_3$	93	164-8	18	1.5352	II
21575	$C_8H_{10}O$	m-methyl-	3-CH_3	71	111-22	25	1.5320	I
30038	$C_{12}H_{16}O_2$	3-allyl-4-ethoxy-	3-$CH_2CH=CH_2$-4-OC_2H_5	95	155-66	14	1.5335	III

Table 4.--Continued

ENT No.	Empirical formula	Substituent	R	Yield %	Boiling point °C.	Boiling point mm.	n_D^{25}	Method of preparation
30040	$C_{11}H_{14}O_2$	3-allyl-4-methoxy-	3-$CH_2CH{=}CH_2$-4-OCH_3	90	158-62	14	1.5443	III
30164	$C_{11}H_{14}O_3$	2-allyloxy-3-methoxy-	2-$OCH_2CH{=}CH_2$-3-OCH_3	52 1/	146-67	19	1.5348	IV
30165	$C_{11}H_{16}O_3$	3-methoxy-2-propoxy-	2-OC_3H_7-3-OCH_3	54	127-48	19	1.5182	2/
30291	$C_{12}H_{16}O_2$	3-methoxy-4-(2-methylallyl)-	3-OCH_3-4-$CH_2C(CH_2){-}CH_3$	85	123-5	0.8	1.5393	II
30293	$C_{11}H_{14}O_2$	o-(2-methylallyloxy)-	2-$OCH_2C(CH_2){-}CH_3$	89 3/	100-14	.4	1.5355	IV
		Benzyl acetates	R—C6H4—CH_2OOCCH_3					
21160	$C_{11}H_{14}O_2$	2,4-dimethyl-	2,4-$(CH_3)_2$	77	123-5	12	1.5049	I
21161	$C_{11}H_{14}O_3$	p-ethoxy-	4-OC_2H_5	68	146-50	16	1.5051	I
21282	$C_{11}H_{14}O_2$	3,4-dimethyl-	3,4-$(CH_3)_2$	57	128	15	1.5050	I
21527	$C_{11}H_{14}O_2$	p-ethyl-	4-C_2H_5	--	120-7	31	1.5006	I
21534	$C_{11}H_{14}O_2$	2,5-dimethyl-	2,5-$(CH_3)_2$	--	130-44	18	1.5043	I
21537	$C_{10}H_{12}O_2$	o-methyl-	2-CH_3	--	120-41	24	1.5083	I
21554	$C_{10}H_{12}O_2$	m-methyl-	3-CH_3	--	109-29	18	1.5035	I
21902	$C_{11}H_{14}O_2$	m-ethyl-	3-C_2H_5	43	120-40	18	1.5062	I

1/ Based on ester starting material.
2/ Hydrogenation of ENT-30164.
3/ Based on aldehyde starting material.

Table 5.--Miscellaneous intermediates

ENT No.	Empirical formula	Intermediate	Yield %	Boiling point		n_D^{25}	Method of preparation
				°C.	mm.		
20884	C_8H_9Br	m-Xylene, alpha-bromo-	58	95-115	15	--	I
20885	$C_9H_{11}Cl$	Toluene, alpha-chloro-4-ethyl-	23	102-15	17	1.5294	I
21872	$C_{13}H_{18}O_3$	m-Toluic acid, 2-ethoxy-, propyl ester	82	90-94	0.7	1.5050	II
30205	$C_{12}H_{10}O_3$	2-Naphthoic acid, 3-hydroxy-, methyl ester	99	m.p. 72-74			II
30207	$C_{15}H_{14}O_3$	2-Naphthoic acid, 3-allyloxy-, methyl ester	78	135	0.2	1.6146	II
30292	$C_{12}H_{12}O_2$	2-Naphthalenemethanol, 3-methoxy-	89	100-14	0.4	1.5355	--

Table 6.--Results of screening tests on substituted benzyl chrysanthemumates and intermediates

(Procedures and activity classifications given by King (9). Numbers indicate relative effectiveness--1 the least effective, 4 or 4A the most effective.)

ENT No.	Mosquito larvicide[1/]	Chigger toxicant[2/]	Body louse toxicant[3/]	Mosquito repellent[4/]
20884	1	1	1	-
20885	2	1	1	1
21001	1	3	1	1
21002	1	3	1	2
21009	1	2	3	1
21159	1	2	4	2
21160	1	2	2	1
21161	1	3	1	1
21170	4	1	4A	1
21171	2	2	1	1
21173	4	1	1	1
21282	1	2	2	1
21300	2	2	1	2
21310	1	2	2	1
21333	1	2	1	3
21335	1	3	3	1
21340	4	1	2	1
21342	4	1	2	1
21413	1	3	3	1
21414	1	2	3	1
21415	1	3	3	1
21416	1	3	2	1
21417	2	3	2	4
21418	1	2	1	1
21419	2	3	3	2
21420	2	2	1	3
21421	2	2	1	4
21422	4	1	4A	1
21423	2	1	1	1
21424	4	1	1	1
21425	2	1	1	1
21426	4	1	4A	1
21427	4	1	1	1
21527	2	3	1	1
21530	1	4	3	1
21534	1	3	2	1
21535	1	2	1	2
21536	1	2	1	2
21537	2	3	1	2
21551	1	3	2	1
21552	1	3	2	1
21553	1	3	3	2
21554	1	2	1	1

Table 6.--Continued

ENT No.	Mosquito larvicide[1]	Chigger toxicant[2]	Body louse toxicant[3]	Mosquito repellent[4]
21555	1	2	1	3
21556	1	1	1	1
21558	4	3	4A	1
21559	4	4A	4A	1
21560	2	1	1	1
21562	1	4	3	1
21563	4	3	1	1
21564	4	1	4A	1
21572	4	2	1	1
21573	4	3	4	1
21575	1	2	1	2
21577	1	2	1	1
21578	1	2	1	1
21704	1	3	4A	1
21705	1	3	2	1
21825	4	1	4	1
21872	1	2	2	1
21902	1	1	1	1
21906	4	1	1	1
30035	2	-	2	-
30036	2	-	2	-
30038	-	-	-	1
30039	4	1	1	1
30040	-	4	-	1
30041	4	1	1	1
30042	2	4	1	1
30164	1	4	1	3
30165	1	4	1	1
30166	1	1	1	1
30167	2	4	1	1
30205	2	3	1	1
30207	2	1	1	1
30230	1	2	1	1
30231	1	4	1	1
30232	1	3	1	1
30239	2	4	1	1
30253	1	4	1	1
30254	1	1	1	1
30291	1	4	1	2
30292	1	1	1	1
30293	1	4	1	2
30298	4	1	3	1
30299	1	4	1	1
30300	4	2	4A	1
30302	1	1	1	1

1/ *Anopheles quadrimaculatus* Say
2/ *Trombicula splendens* Ewing
3/ *Pediculus humanus humanus* L.
4/ *Aedes aegypti* (L.)